



# THE CITY OF NEW YORK

DEPARTMENT OF HEALTH AND MENTAL HYGIENE

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## **DOHMH Alert #7: Primary 3-Drug-Class-Resistant HIV-1 Infection with rapid CD4+ T cell depletion and progression to AIDS in a New York City Man who has Sex with Men**

- Primary infection with 3-drug-class-resistant HIV-1 accompanied by apparently rapid CD4+ T cell depletion and progression to AIDS has been confirmed in a New York City man who has sex with other men (MSM), who reports frequent episodes of unprotected anal intercourse with men, often accompanied by crystal methamphetamine use.
- Evaluation of patients with HIV risk factors presenting with symptoms consistent with acute retroviral syndrome should include tests for HIV infection **both** by serology and tests for HIV nucleic acid (e.g. HIV-1 RNA PCR or bDNA). For all persons with newly diagnosed HIV infection and all previously untreated HIV-positive persons, obtain drug resistance testing.
- This incident highlights the need to improve patient adherence to antiretroviral treatment to prevent further development and spread of drug resistance.
- Obtain partner names and contact information from HIV-positive persons and provide or refer for HIV testing. Persons with recent HIV infection have enhanced transmission efficiency due to high viral loads. Identifying potentially infected partners helps stop HIV transmission.
- Call the Contact Notification Assistance Program (212-693-1419) at the Health Department for assistance with partner notification. The Health Department can work with HIV-positive patients to identify sex and needle sharing partners, notify partners of HIV exposure without disclosing any original patient information, and ensure access to free HIV testing and referral for any necessary medical and social services.

**Please distribute to colleagues in HIV Primary Care, Infectious Disease, Emergency Medicine, Family Practice, Internal Medicine, Primary Care, Neurology, Laboratory Medicine, Obstetrics/Gynecology, Pediatrics, and Adolescent Medicine.**

Dear Colleague:

In January 2005, a New York City man was diagnosed with primary HIV infection with 3-drug-class-resistant HIV-1 (3DCR HIV) with apparently rapid progression to AIDS by Dr. Martin Markowitz and colleagues at the Aaron Diamond AIDS Research Center (ADARC). The patient is a man who has sex with men (MSM) who reports crystal methamphetamine use and unprotected insertive and receptive anal intercourse with multiple partners, including partners

identified through anonymous Internet contacts in mid-October 2004. The patient last tested negative for HIV-1 in May 2003. He had symptoms of acute retroviral syndrome (fever, fatigue, and pharyngitis) during early November 2004. He tested positive for HIV-1 by serology on Dec.16, 2004. By January, when he presented with weight loss (4 kg), continued fatigue and malaise, he had a low CD4 count ( $<100$  cells/mm<sup>3</sup>) and elevated viral load.

Genotypic and phenotypic testing demonstrate that the patient's virus is resistant to three classes of anti-viral drugs: nucleoside or nucleotide reverse transcriptase inhibitors (NRTI), non-nucleoside reverse transcriptase inhibitors (NNRTI), and protease inhibitors (PI). The strain appears to be susceptible to T-20 (enfuvirtide, Fuzeon) and may be susceptible to efavirenz (Sustiva). The virus appears to be dual-tropic, that is, able to use both CCR5 (R5) and CXCR4 (X4) as co-receptors. HIV variants with tropism for X4 have been associated with rapid disease progression.

Sporadic transmission of highly resistant HIV-1 has been reported previously.<sup>1,2</sup> Recent data from ADARC suggest that the transmission of resistant HIV may be increasing in New York City. In a cohort followed at ADARC consisting primarily of men who have sex with men, NNRTI resistance in treatment-naïve, recently infected persons rose from 2.6% to 14.3%, and resistance to 2 or more classes of antiretroviral drugs increased from 2.6% to 9.8% between 1995-1998 and 2003-2004. Increasing drug resistance makes HIV treatment more complex and may worsen prognosis.

This case, along with rising syphilis rates and recent reports of lymphogranuloma venereum (LGV) in HIV+ MSM, reflects a high level of unsafe sex in the MSM community. Providers should counsel HIV-infected and uninfected men at risk to reduce unsafe sexual behavior and should address drug use and mental health problems. Providers should increase HIV testing and ensure that partners are identified, notified and tested. Substance abuse, including methamphetamine and cocaine use, is associated with increased sexual risk taking. There is an urgent need to improve adherence among patients receiving antiretroviral treatment in order to prevent further development and spread of drug-resistant HIV. Adherence improves with simpler regimens, housing support, mental health services, and drug and alcohol treatment.

The identification of a case of primary HIV infection that is resistant to many available antiretroviral agents and associated with rapid progression to AIDS in a person in the MSM, methamphetamine-using population is of great public health concern. Although neither this patient's precise course, nor the extent of dissemination of this strain, is known at this time, there is a potential for widespread dissemination of this highly resistant, rapidly progressive HIV strain, particularly in the MSM community. The extent of drug resistance in NYC is not known because of the lack of a surveillance system to monitor drug resistance patterns. We are working with New York State to improve surveillance for drug resistance in treatment-naïve and newly diagnosed HIV-infected patients.

Because this 3DCR HIV strain may become more prevalent in NYC, the Department of Health and Mental Hygiene (DOHMH) recommends that providers:

1. Consider acute retroviral syndrome among patients who may have risk factors for recent HIV infection. Acute retroviral syndrome is a flu-like illness which may include fever, lymphadenopathy, pharyngitis, rash, myalgias, diarrhea, headache, nausea and vomiting, hepatosplenomegaly, weight loss, thrush, and neurologic symptoms lasting one to two weeks, generally within 1-2 months of risk behavior. Obtain a thorough risk factor history and, for all persons who have such a history and symptoms consistent with acute retroviral syndrome, test for HIV infection **both** by serology and tests for HIV nucleic acid (e.g., HIV-1 RNA PCR or bDNA).
2. Test for drug resistance in all persons with newly diagnosed HIV. Genotypic assays detect resistance-conferring mutations. Phenotypic assays directly measure resistance of the patient's HIV strain to specific individual drugs. If you suspect that a patient has been infected with 3DCR HIV, report the case immediately to the DOHMH's Bureau of HIV/AIDS Prevention and Control at (212) 442-3388.
3. Drug resistance testing should also be obtained, along with a careful assessment of patient adherence, in all cases of clinical deterioration, incomplete viral suppression, or virologic failure. Use results of resistance testing to guide treatment.
4. Ensure adherence among patients receiving antiretroviral treatment in order to prevent further development and spread of drug-resistant HIV. Adherence improves with simpler regimens, housing support, mental health services, and drug and alcohol treatment.
5. Obtain, or refer to the DOHMH to obtain, partner names and contact information from all persons testing HIV+. Notify partners and recommend or obtain HIV testing; for HIV antibody-negative persons with symptoms of acute seroconversion, additional testing for HIV nucleic acid (e.g., HIV-1 RNA PCR or bDNA) is indicated. Persons with primary HIV infection have enhanced transmission efficiency due to their high viral loads. Partner notification results in prompt diagnosis of HIV and reduces spread of HIV; HIV-positive persons who are aware of their status are much more likely to reduce risky behavior. Call the DOHMH's Contact Notification Assistance Program (212) 693-1419 for assistance with partner notification. For more information on partner notification, see <http://www.nyc.gov/html/doh/pdf/chi/chi23-7.pdf>.

As always, we appreciate our partnership with the medical community in recognizing and responding to this emerging infectious disease threat.

Sincerely,

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<sup>1</sup> Boden D, Hurley A, Zhang L, Cao Y, Guo Y, Jones E, Markowitz M, et al. HIV-1 drug resistance in newly infected individuals. JAMA 1999; 282:1135–1141.

<sup>2</sup> Little SJ, Holte S, Routy JP, Daar ES, Markowitz M, Collier AC, et al. Antiretroviral-drug resistance among patients recently infected with HIV. N Engl J Med 2002; 347:385–394.